UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,585	07/26/2001	Klaas Poelstra	POELSTRA	2750

545 7590 06/03/2004

ANTHONY H. HANDAL
KIRKPATRICK & LOCKHART, LLP
599 LEXINGTON AVENUE
31ST FLOOR
NEW YORK, NY 10022-6030

EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,585	POELSTRA ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 36-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 36-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is response to Applicant's amendment and response filed February 17, 2004. Claims 1-10, 12-14, 16, 18, 20-23 and 36 have been amended. Claims 24-35 have been cancelled. Claims 37-44 have been added.

Rejections Withdrawn

2. In view of Applicant's amendment and response the following objections/rejections have been withdrawn:

a) objection of claim 1, page 3, paragraph 2 of the previous Office action.

b) rejection of claims 1-23 and 36, page 3, paragraph 3 of the previous Office action.

c) rejection of claims 1-23 and 36, page 3, paragraph 4 of the previous Office action.

d) rejection of claim 21, page 4, paragraph 5, of the previous Office action.

e) rejection of claim 13, page 5, paragraph 6, of the previous Office action.

f) rejection of claims 1-23 and 36, paragraph 7 of the previous Office action.

New Grounds of Rejection

Claims Objections

3. Claim 9 should end in a period (.). Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification teaches that modifications of LPS and other lipid A like structures can be made by using recombinant techniques (page 3). The specification broadly describes a genus of compounds that have no structural description

accompanying the variant language (i.e. chemically modified or genetically modified derivatives of natural LPS binding site binding substances) recited in the claims. None of these sequences meet the written description provision of 35 U.S.C. 112, first, paragraph. While recombinant techniques are known in the art, it is not routine in the art to screen for multiple substitutions or multiple modifications of any compound and the result of such modifications is unpredictable based on the instant disclosure. Therefore, only LPS and not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of LPS, the skilled artisan cannot envision the detailed chemical structure of the encompassed compound regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d

1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, LPS and not chemically modified or genetically modified derivatives of natural LPS binding site binding substances) meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-23 and 36-44 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. See the comments below:

a) claims 1 recites "attributable" and "derived from". It is unclear as to what Applicant is referring to? Correction is required.

b) claims 2 recites "equivalent sample". It is unclear as to what Applicant is referring to? Correction is required.

c) claim 7 recites "chemically modified or genetically modified derivatives of natural LPS binding site binding substances". It is unclear as to what Applicant is referring to? Correction is required.

d) claims 13 recites "optionally" and "suitable discriminating entities". It is unclear as to what Applicant is referring to? In regard to the recitation of optionally, claim limitations must be positively recited in the claims. Correction is required.

e) claims 15 recites a sample from the patient for another disease related to the increase of alkaline phosphatase activity". It is unclear as to what Applicant is referring to? Correction is required.

f) claims 1-23 and 36-44 "monitoring the degree of LPS binding sites on alkaline phosphatase in a sample fluid". It is unclear as to what Applicant is referring to? Correction is required.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-23 and 36-44 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious Poelstra et al *(American Journal of Pathology, Vol. 151, No. 4, October 1997).*

Claims 1-23 and 36-44 are drawn to a method of diagnosis of onset of endotoxemia or sepsis attributable to a gram-negative bacterial infection said method comprising monitoring the degree of occupancy of lipopolysaccharide binding sites on alkaline phosphatase in a sample of fluid derived from a patient wherein the degree of occupancy is associated with the presence or absence of gram-negative bacterial infection.

Poelstra et al teach a method of monitoring the degree of occupancy of lipopolysaccharide binding sites on alkaline phosphatase in a sample derived from a patient (page 1164, 2nd column). Poelstra et al disclose the survival time of rats after administration of bacteria *(E. coli or S. minnosota*) or levamisole or both (figure 3). Poelstra et al teach that LPS from both *E. coli or S.* ~~*minnesota*~~ minnesota was dephosphorylated at a physiological pH level by phosphatase activity in intestinal cryostat section (page 1167). Poelstra et al teach that measured enzyme activity was shown to be due to AP because of the localization of the reaction product corresponding exactly with AP activity (page 1167). Poelstra et al do not specifically disclose a method of diagnosis of onset of endotoxemia or sepsis attributable to a gram-negative bacterial infection said method comprising monitoring the degree of occupancy of lipopolysaccharide binding sites on alkaline phosphatase in a sample of fluid derived

from a patient. However, Poelstra et al teach that elevated AP level are found in both serum and in liver (page 1168). Claim limitations such as "a sample is taken from an individual both prior to and following trauma or shortly after having undergone trauma wherein the trauma comprises surgery, burns or ischemic traumas", "wherein the sample is taken from an individual during hospitalization", "wherein the number of times during a period of time and the data are compared to reveal the degree of alkaline phosphatase binding site occupancy over time", "wherein the period of time is as long as the individual is at risk of infection i.e. during hospitalization or post trauma recovery, during illness, injury, pregnancy, hospitalization and post tram recovery", "wherein the group of individuals consists of a patient, an individual at risk of gram-negative infection prior to trauma and a hospitalized patient", "wherein multiple alkaline phosphatase activity determinations are made during a period of time and the data are compared to reveal the activity level over time" and "wherein the sample is a cholestasis-free patient or cholestasis-free patient at risk of gram-negative bacterial infection, a cholestasis-free patient prior to or after trauma or a hospitalized cholestasis-free patient"are being viewed as optimizing experimental parameters.

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to monitor the degree of occupancy of lipopolysaccharide binding sites on alkaline phosphatase in a sample of fluid derived from a patient wherein the degree of occupancy is associated with the presence or absence of gram-negative bacterial infection because Poelstra et al teach that elevated AP level are found in both serum and in liver (page 1168). It would be expected barring evidence to the contrary

that monitor the degree of occupancy of lipopolysaccharide binding sites on alkaline phosphatase in a sample of fluid would be associated with the presence or absence of gram-negative bacterial infection because Poelstra et al teach that endotoxin is a natural substrate for AP and enhanced AP activity observed during disease reflects a physiological response of the liver upon bile duct obstruction (page 1168).

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
May 26, 2004

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600